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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,974	RAUTH ET AL.	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-89* is/are pending in the application.

4a) Of the above claim(s) *72-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed May 19, 2004 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1-44 have been canceled.

Claims 45-89 have been added.

Remarks drawn to rejections of Office Action mailed January 20, 2004 include:

112 2nd paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

102(b) rejections: which have been maintained for reasons of record.

An action on the merits of claims 45-89 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Newly submitted claims 72-89 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: these claims are correlative to the previous claims 27-37 and 39-44, which were withdrawn as they were restricted in restriction requirement set forth on 9/4/2003.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, claims 72-89 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

Claim 63 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim intends to limit step (d) of the method of claim 59, however, claim 59 does not have a step (d). It appears the claim should depend from claim 60. Applicants should also include the alphanumerical indicator, i.e., "(d)", to claim 60 to provide proper antecedent basis for the use of "(d)".

Likewise, claims 64-65 are seen to be improperly dependent upon claim 59, wherein it appears they should properly depend from claim 60.

Claim Rejections - 35 USC § 102

Claims 45, 46, and 48-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628) for the same reasons that claims 1, 2, and 4-13 were previously.

Claim 45 of the instant application is drawn to a method of binding nucleic acids to a solid phase comprising: contacting a solution containing nucleic acids with a solid phase which has hydrophobic and hydrophilic groups on the surface and a binder solution comprising a salt and polyethylene glycol, whereby the nucleic acids reversibly and sequence-unspecifically bind to the surface of the solid phase. Claim 46 provides that the hydrophobic groups are alkyl or aryl groups. Claim 48 provides that the hydrophilic groups are hydroxyl groups. Claim 49 provides

that the solid phase is solid particles, and claim 50 provides they are magnetic. Claim 51 provides that salt is an alkali, alkaline earth and/or ammonium halide. Claim 52 limits the molar mass of the polyethylene glycol to 1,000-20,000 g/mol. Claim 53 limits the salt concentration to 5 mmol/l to 4 mol/l. Claim 54 provides the concentration of the polyethylene glycol is 5-40% based on the weight. Claim 55 limits the nucleic acid to DNA, and claim 56 provides that the nucleic acid is an amplification product. Claim 57 provides that single- or double-stranded nucleic acids are selectively bound.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23). The magnetic microparticles are taught to be coated with a silane coat, such as n-dodecyltriethoxysilane (comprising an alkyl hydrophobic group) and a functional group such as a carboxyl group or thiol group (both hydrophilic groups) wherein carboxyl groups comprise a hydroxyl group bound to a carbonyl group (column 3, lines 10-55). Hawkins teaches that salts such as NaCl, LiCl, $BaCl_2$, KCl, $CaCl_2$, $MgCl_2$, and CeCl (column 5, lines 46-57) (various alkali and alkaline earth halides). The salt concentration is taught to be from about 0.5M to 5.0M, and the polyethylene glycol is taught to be from about 7-13% while having a molecular weight of from about 6,000-10,000 (column 5, lines 35-65). Hawkins additionally teaches that DNA and PCR amplification products can be used as the nucleic acids (column 6, lines 33-39, example 6). Moreover, the polynucleotide is taught to be either single or double stranded (column 6, lines 60-62).

Applicant's arguments filed May 19, 2004 have been fully considered but they are not persuasive. Applicants argue that Hawkins indicates that the polynucleotides bind to his surface through the hydrophilic groups and that applicant's hydrophilic groups serve a different purpose. However, it is irrelevant of the purpose of the hydrophilic group, as the only thing required by the claims of the instant application is for there to be hydrophobic and hydrophilic groups, which Hawkins does indeed have. Applicants also argue that Hawkins teaches the silane groups have functional groups (carboxyl groups) attached thereto, leading to microparticles which have their entire surface coated with the functional groups. However, the instant applications claims only require that there be hydrophobic and hydrophilic groups on its surface. There is no indication of any other requirement of the groups other than they must be on the surface. Thus, Hawkins silane groups and carboxyl groups are on the surface of their microparticles, and thus meet the limitations of the claims in the instant application.

Claims 59-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628) for the same reasons as claims 15-19 were in the previous office action.

Claim 59 is drawn to a method of isolating or purifying nucleic acids comprising the steps of: contacting a solution containing nucleic acids with a solid phase which has hydrophobic and hydrophilic groups on the surface and a binder solution comprising a salt and polyethylene glycol, whereby the nucleic acids reversibly and sequence-unspecifically bind to the surface of the solid phase, separating the solid phase from the solution, and optionally detaching the nucleic acid from the solid phase. Claim 60 provides that the nucleic acid is detached from the solid phase. Claims 61 and 64 provide that the solid phase is magnetic and the solid phase is separated

(from the nucleic acid) by magnetic means. Claim 62 provides that the solid phase is washed with a buffer solution which detaches impurities bound to the solid phase but not the nucleic acids. Claim 63 provides that the nucleic acids are detached using an elution solution. Claim 65 provides the nucleic acid is subject to a mass spectrometric analysis.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23) as set forth supra. Moreover, Hawkins teaches that nucleic acid bound microparticles can be separated from the supernatant by applying a magnetic field, and once separated from the supernatant, the DNA can be removed from the magnetic microparticles by washing with an elution buffer, wherein the elution buffer comprising the nucleic acids can be separated from the magnetic microparticles by applying a magnetic field (column 6, lines 3-28). Moreover, the magnetic microparticles with bound DNA can be washed with a buffer solution before separating the DNA so that impurities bound to the DNA molecule or microparticle are dissolved and the DNA remains attached to the microparticle (column 6, lines 30-59).

Applicant's arguments and the examiner's responses are set forth supra.

Claims 66-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628) for the same reasons as claims 21-22 were in the previous office action.

Claim 66 is drawn to a method of determining the nucleotide sequence of a nucleic acid comprising binding a nucleic acid to a solid phase by the method of claim 45 as set forth supra,

and additionally by sequencing the nucleic acid by known methods. Claim 67 provides that the sequenced product is then purified.

Hawkins teaches a method of binding polynucleotides non-specifically and reversibly to a solid phase, such as a magnetic microparticle, whose surface is coated with a functional group (column 1, lines 24-28), in combination with a salt and polyethylene glycol (column 2, lines 16-23) as set forth supra. Additionally, Hawkins teaches that the nucleotide sequence bound to the magnetic microparticles can be determined by using conditions suitable for sequence determination which are known in the art (column 8, lines 41-52). Hawkins then teaches to purify the product by electrophoresis (example 5).

Applicant's arguments are the examiner's responses are set forth supra.

Claims 70 and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins (US Patent 5,705,628) for the same reasons as claims 25-26 were in the previous office action.

Claim 70 is drawn to a kit for practicing the method as set forth supra comprising, a binding buffer which contains a salt and polyethylene glycol, and a solid phase which has hydrophobic and hydrophilic groups on its surface. Claim 71 adds an elution buffer to detach the nucleic acid from the surface and a washing buffer to separate the impurities to the kit of claim 70.

Hawkins teaches a kit for practicing the methods as set forth supra comprising the magnetic microparticles as set forth supra with a binding buffer. Moreover, Hawkins teaches there can be additionally an elution buffer to detach the nucleic acid from the solid phase and a wash buffer for removing the impurities (column 8, line 53 – column 9, line 15).

Applicant's arguments and the examiner's responses are set forth supra.

Claim Rejections - 35 USC § 103

Claims 45-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hawkins (US Patent 5,705,628) in view of Tang et al. (5,668,268) for the reasons claims 1-24 were rejected in the previous office action.

Claims 45, 46, 48-57, and 59-67 are drawn to the methods as set forth supra. Claim 47 further limits the method of claim 46 by stating that the alkyl groups of claim 46 are preferably C_8 or C_{18} alkyls, or mixtures thereof. Claim 58 provides that the nucleic acids are preferably in the range of from 5-1000 nucleotides. Claim 68 is drawn to a method of synthesizing nucleic acids comprising binding a nucleic acid to a solid phase as in claim 45, then extending the nucleic acid by known methods. Claim 69 is drawn to a method of detecting an analyte in a sample comprising attaching a nucleic acid to a solid phase as set forth supra, the contacting the solid phase with an analyte and determine if the analyte bound to the nucleic acids.

It is noted that these additional limitations are not seen to be critical and obvious to one of ordinary skill in the art. Applicant's method of claim 68 which comprises "extending the nucleic acid by at least one nucleotide by known methods", for example, shows that nothing is added to the claim which is not already known in the art. Additionally, the use of the C_8 or C_{18} alkyl groups is not seen to be critical, but merely optimizing an art recognized method. There are no data or examples in the disclosure which would afford the skilled artisan evidence that these limitations are anything more than a preferred embodiment of the prior arts known methods. Additionally, Hawkins is silent to the length of the nucleic acids, however, they do clearly state

that nucleic acids can be separated based on size (column 7, lines 18-55) wherein Hawkins indeed contemplates the fact that various nucleic acids are eluted at varying polyethylene glycol concentrations. Moreover, the method of claim 69 is seen to be an obvious variant to the method of Hawkins, as analytes are known to be any chemical substance which is to be analyzed, and one of skill in the are would recognize and understand methods of detecting an analyte using the method of Hawkins.

It is noted that applicants main focus is seen to be the use of both hydrophobic and hydrophilic functional groups attached to a magnetic microparticle, and subsequent attachment of nucleic acids while in a solution of polyethylene glycol and a salt. Hawkins renders this method obvious since a compound and its properties are inseparable. To use a compound in a manner to exploit its properties is prima facia obvious. Moreover, the examiner would like to make of record Tang et al. (US Patent 5,668,268) which teaches methods of synthesizing and purifying oligonucleotides wherein a plurality of microparticles which have hydroxyl or amino groups are utilized which have had some of the hydrophilic hydroxyl or amino groups modified to hydrophobic groups by attaching a phenyl group to a portion of the hydrophilic hydroxyl or amino groups.

The claims of the instant application must contain new and patentable measures over the prior art to be patentable.

Applicant's arguments filed May 19, 2004 have been fully considered but they are not persuasive. Applicants argue that Hawkins does not disclose both hydrophilic and hydrophobic

groups on its surface and that Tang does not remedy this deficiency. However, as set forth supra, Hawkins does have both hydrophobic and hydrophilic groups on its carboxyamino silane functionalized surface.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
October 1, 2004

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623